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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,360	12/22/2003	Stavros C. Manolagas	3650.1004-008	9347

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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/743,360	MANOLAGAS ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-3 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 22 December 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 7/9/04 & 8/16/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 are pending in the instant application.

This application claims benefit of priority as a continuation of U.S. Application No. 09/413,785, filed October 7, 1999, now abandoned.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 09/413,785, 60/116,409, and 60/103,385, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Claims 1-3 recite the limitation of "at least 10 micrograms per kilogram body weight" but the earlier-filed applications do not provide support for this particular dosage range, with a lower limit, but no upper limit. The earlier-filed applications only provide support for a dosage of "about 10 μg/kg of body weight to about 1000 μg/kg of body weight" (see page 16, lines 9-11 of Application No. 09/413,785).

While it is noted that the instant application only provides support for the "at least 10 micrograms per kilogram body weight" limitation in the claims, with no antecedent basis in the description portion of

the specification, it is acknowledged that claims reciting this limitation were present in the application on the filing date (December 22, 2003).

Specific reference to the prior-filed application. This application claims benefit of priority as a continuation of U.S. Application No. 09/413,785, filed October 7, 1999, now abandoned. For the reasons set forth above, this application is actually a continuation-in-part of U.S. Application No. 09/413,785. Applicant is required to amend the first sentence of the specification to indicate the proper relationship to the parent case, which is a continuation-in-part.

If Applicants wish the instant application to be accorded status as a continuation application, the subject matter that is not supported by parent case 09/413,785 must be removed from the specification, including the claims. In that case, a new oath/declaration would not be required.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration has reviewed and understands the contents of the specification, including the claims, as amended by any amendment specifically referred to in the oath or declaration.

Applicants have filed a copy of the declaration filed in parent case 09/413,785. However, since this application is a continuation-in-part, instead of a continuation application, a new oath or declaration identifying the instant specification and claims, along with the surcharge set forth in 37 CFR 1.16, is required. See MPEP § 602.05(a).

Information Disclosure Statement

The information disclosure statement filed July 9, 2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the citation of reference no. AT8 (Lane et al.) does not provide the title of the publication and therefore it is unclear what is being cited. See MPEP § 609.05(a). The citation has been lined through and a citation to what appears to be the same reference has been provided by the Examiner on the PTO-892.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification lacks antecedent basis for a dosage of "at least 10 micrograms per kilogram body weight" as recited in Claim 1.

This objection may also be overcome by removing the limitation from the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lane et al. (September 1997, Arthritis and Rheumatism 40(9 Suppl.): S324, Abstract No. 1757).

The claims are directed to a method of increasing the lifespan of osteoblasts in a bone-containing host in need of preventing bone loss or stimulating bone formation, wherein the host is currently being treated with one or more glucocorticoid compounds or the host is experiencing adverse bone effects resulting from contact with one or more glucocorticoid compounds, comprising the steps of administering at least 10 μg per kilogram body weight of isolated parathyroid hormone fragment (1-34).

While the preamble of the claims recite "increasing the lifespan of osteoblasts," this phrase is given no patentable weight, as the specification clearly discloses that the purpose of administering PTH is to stimulate bone formation (page 18, lines 17-20 of specification).

Lane et al. (1997) disclose a randomized controlled clinical trial where postmenopausal women on chronic glucocorticoid treatment were treated with daily human parathyroid hormone (1-34). The parathyroid hormone (PTH) was administered at 400 IU/day for 1 year. Daily PTH therapy dramatically increased spinal trabecular bone mass.

Since the steps carried out are substantially identical to that which is claimed, the effect of "increasing the lifespan of osteoblasts" is presumed inherent to the method as claimed. The MPEP states that the "express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103." MPEP § 2112. Also see the decision of *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) which states that "[t]he inherent teaching of a

prior art reference, a question of fact, arises both in the context of anticipation and obviousness." The MPEP further emphasizes that the "inherent feature need not be recognized at the time of the invention" (MPEP § 2112).

Although the reference does not provide the dosage in terms of micrograms PTH per kilogram body weight, it does report a dose of 400 IU/day and further teaches that the regimen resulted in increased spinal trabecular bone mass. The term IU (i.e., international units) is a measure of the biological activity of a specific preparation of a compound. Therefore, some preparations may have a relatively high number of international units per mg of the preparation, whereas other preparations, containing a higher percentage of inactive material (e.g., denatured protein), may have a lower number of international units per mg of preparation. As such, even if the dose of 400 IU does not correlate to a dosage of "at least 10 micrograms per kilogram body weight," it would have been obvious to one of skill in the art to determine the workable dosing range for increasing bone mass, stimulating bone formation, or preventing bone loss. It would have been *prima facie* obvious to one of skill in the art to perform routine experiments to determine the workable ranges for the dosage of PTH(1-34) to arrive at doses that achieve the desired effect of increasing bone mass or preventing bone loss. See *In re Aller*, 105 USPQ 233 at 235 (CCPA 1955), which states "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Also see MPEP § 2144.05.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention or anticipated by the cited reference.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lane et al. (1995, J. Bone and Mineral Res. 10(10):1470-1477) and U.S. Patent No. 5,821,225 (Vickery, filed June 7, 1995).

The claims are directed to a method of increasing the lifespan of osteoblasts in a bone-containing host in need of preventing bone loss or stimulating bone formation, wherein the host is currently being

treated with one or more glucocorticoid compounds or the host is experiencing adverse bone effects resulting from contact with one or more glucocorticoid compounds, comprising the steps of administering at least 10 μg per kilogram body weight of isolated parathyroid hormone fragment (1-34).

Lane et al. (1995) disclose that intermittent administration of hPTH(1-34) at 40 μg/kg body weight and 400 μg/ kg body weight, to osteopenic rats, resulted in increased trabecular bone volume (Abstract and page 1471, column 2, paragraph 1). The reference further discloses that intermittent PTH injections appear to increase bone mass by adding bone to existing trabeculae (page 1470, column 2, paragraph 1). Thus, an increase in trabecular bone volume would clearly correlate with an increase in bone mass.

Vickery (1995) discloses that corticosteroid induced osteopenia and osteoporosis was well known in the art and refers to several publications pertaining to the subject (columns 1-2). The reference further discloses synthetic polypeptide analogs of parathyroid hormone that are useful for the treatment of corticosteroid-induced osteopenia in mammals.

While the preamble of the claims recite "increasing the lifespan of osteoblasts," this phrase is given no patentable weight, as the specification clearly discloses that the purpose of administering PTH is to stimulate bone formation (page 18, lines 17-20 of specification). Since the steps carried out are substantially identical to that which is claimed, the effect of "increasing the lifespan of osteoblasts" is presumed inherent to the method as claimed. The MPEP states that the "express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103." MPEP § 2112. Also see the decision of *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) which states that "[t]he inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." The MPEP further emphasizes that the "inherent feature need not be recognized at the time of the invention" (MPEP § 2112).

Since one of skill in the art would have been motivated to treat osteoporosis in its various forms, given the combined teachings of Lane et al. and Vickery, the skilled artisan would have realized that there

was a need to prevent the bone loss that accompanies corticosteroid use and would have been motivated to use the method disclosed by Lane et al. to treat corticosteroid-induced osteoporosis by administration of PTH(1-34), particularly in view of the teaching of Lane et al. that treatment with intermittent PTH91-34) "has been shown to significantly increase bone mass in osteoporotic animals and humans" (p. 1470, column 2, paragraph 1). The skilled artisan would have anticipated a reasonable expectation of success because the method had already been shown to be effective in increasing bone mass in osteoporotic animals and humans. Thus, one of skill in the art would have been motivated to combine the teachings of Lane et al. (1995) and Vickery (1995) to treat patients with glucocorticoid-induced osteoporosis.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lane et al. (1995, J. Bone and Mineral Res. 10(10):1470-1477), U.S. Patent No. 5,821,225 (Vickery, filed June 7, 1995), and Finkelstein et al. (1994, The New England Journal of Medicine 331(24): 1618-1623).

The claims are directed to a method of increasing the lifespan of osteoblasts in a bone-containing host in need of preventing bone loss or stimulating bone formation, wherein the host is currently being treated with one or more glucocorticoid compounds or the host is experiencing adverse bone effects resulting from contact with one or more glucocorticoid compounds, comprising the steps of administering at least 10 μg per kilogram body weight of isolated parathyroid hormone fragment (1-34), wherein the host is a human.

Lane et al. (1995) disclose that intermittent administration of hPTH(1-34) at 40 μg/kg body weight and 400 μg/ kg body weight, to osteopenic rats, resulted in increased trabecular bone volume (Abstract and page 1471, column 2, paragraph 1). The reference further discloses that intermittent PTH injections appear to increase bone mass by adding bone to existing trabeculae (page 1470, column 2,

paragraph 1). Thus, an increase in trabecular bone volume would clearly correlate with an increase in bone mass.

Vickery (1995) discloses that corticosteroid induced osteopenia and osteoporosis was well known in the art and refers to several publications pertaining to the subject (columns 1-2). The reference further discloses synthetic polypeptide analogs of parathyroid hormone that are useful for the treatment of corticosteroid-induced osteopenia in mammals.

Finkelstein et al. (1994) disclose a method for preventing bone loss in humans by the subcutaneous administration of parathyroid hormone-(1-34). The dose disclosed by Finkelstein et al. is 40 μg, administered subcutaneously (abstract). The reference discloses that the regimen prevents bone loss (abstract and Figure 1).

While the preamble of the claims recite "increasing the lifespan of osteoblasts," this phrase is given no patentable weight, as the specification clearly discloses that the purpose of administering PTH is to stimulate bone formation (page 18, lines 17-20 of specification). Since the steps carried out are substantially identical to that which is claimed, the effect of "increasing the lifespan of osteoblasts" is presumed inherent to the method as claimed. The MPEP states that the "express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103." MPEP § 2112. Also see the decision of *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) which states that "[t]he inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." The MPEP further emphasizes that the "inherent feature need not be recognized at the time of the invention" (MPEP § 2112).

Since one of skill in the art would have been motivated to treat osteoporosis in its various forms, given the combined teachings of Lane et al. and Vickery, the skilled artisan would have realized that there was a need to prevent the bone loss that accompanies corticosteroid use and would have been motivated to use the method disclosed by Lane et al. to treat corticosteroid-induced osteoporosis by administration of PTH(1-34), particularly in view of the teaching of Lane et al. that treatment with intermittent PTH91-

34) "has been shown to significantly increase bone mass in osteoporotic animals and humans" (p. 1470, column 2, paragraph 1). Although Finkelstein et al. (1998) disclose low dose administration of the parathyroid hormone fragment by subcutaneous injection, one of skill in the art would have readily recognized that Lane et al. discloses that doses of 40 μg/kg body weight and 400 μg/ kg body weight resulted in increased bone mass. Thus, only routine experimentation would have been required to extend the invention of Finkelstein et al. from the subcutaneous mode of administration to other modes of administration as described by Lane et al. Furthermore, one of skill in the art would have recognized that the disclosure of Lane et al. in combination with Finkelstein et al. demonstrates that doses of PTH(1-34) that are significantly higher than that used by Finkelstein et al. are effective in increasing bone mass. The skilled artisan would have anticipated a reasonable expectation of success because the method had already been shown to be effective in increasing bone mass in osteoporotic animals and humans. Thus, one of skill in the art would have been motivated to combine the teachings of Lane et al. (1995), Vickery (1995), and Finkelstein et al. (1998) to treat patients with glucocorticoid-induced osteoporosis.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

No claims are allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER